

REMARKS

Overview

In the Office Action under reply, the following rejections have been set forth:

Claims 14-24, and 54-58 stand rejected under 35 USC § 102 as being anticipated by:

1. Fuerstner et al., *Angew Chem Int Ed*, 1995, 34(6): 678-681
2. Black et al., *J Chem Soc*, 1993, v10, 819-821
3. Pindur et al., *J Heterocyclic Chem*, 1987, 24(1), 159-163
4. Chu et al., *J Heterocyclic Chem*, 1984, 21(6) 1901-1903
5. Brieskorn et al., *Archiv der Pharmazie* (Weinheim, Germany), 1979, 312(12), 1046-1051
6. Hindo et al., *Chem & Pharm Bull*, 1974, 22(11), 2728-2731
7. Suzuki et al., *Chem & Pharm Bull*, 1973, 21(12), 2739-2748
8. Hill et al. *J Chem Soc, Perkin Trans 1: Org and Bio-Org Chem* (1972-1999), 1972, (9-10):1210-1219.

The above rejections are addressed in part by the present amendments and are otherwise traversed by the arguments set forth below.

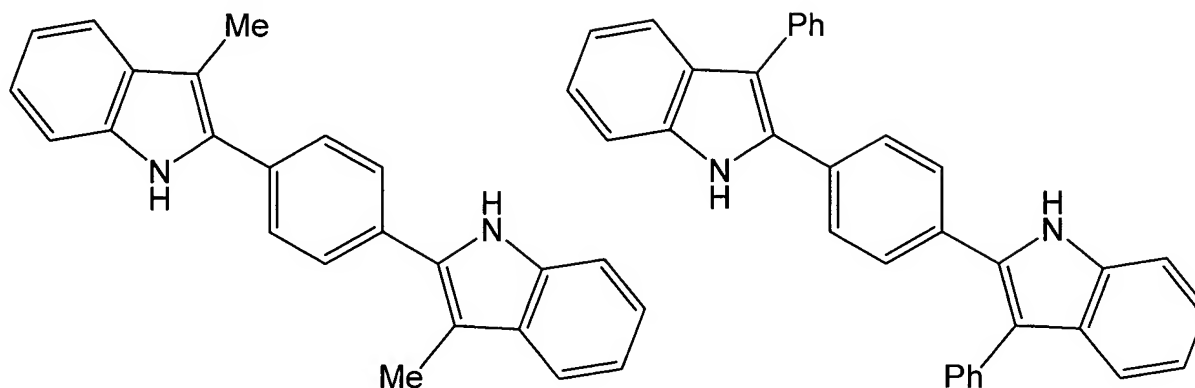
Amendments to the Claims and Claims Status

By the foregoing amendment, claim 14 has been amended to recite that "at least one of R² and R⁶ is other than hydrogen." No new matter has been added, since support for this amendment follows from the claim language itself and from the description in the specification.

Newly added claim 124 is directed toward a pharmaceutical composition comprising a pharmaceutically acceptable carrier in combination with a compound having the structure of formula (IIb). Support for this claim follows from the original claim language as well as the description in the specification.

Rejection under 35 U.S.C. § 102

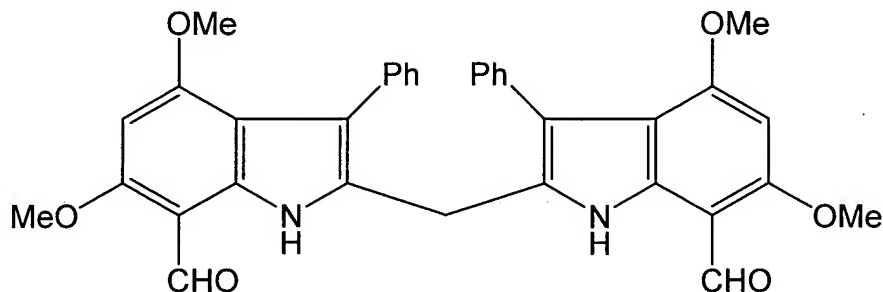
Claims 14-24 and 54-58 stand rejected under 35 U.S.C. §102 as being anticipated by Fuerstner et al., the Examiner citing the two compounds 1H-Indole, 2,2'-(1,4-phenylene)bis[3-phenyl-, and 1H-Indole, 2,2'-(1,4-phenylene)bis[3-methyl-, which have the following structures:



The present claims do not read on the compounds in Fuerstner. The variables R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , and R^8 all represent hydrogen for each of the compounds from the reference, whereas claims 14-24 and 54-58 of the application require that at least one of R^2 and R^6 be other than hydrogen. Accordingly, Fuerstner does not anticipate the current claims, and removal of the rejection under 35 USC § 102 is respectfully requested.

Rejection under 35 U.S.C. § 102

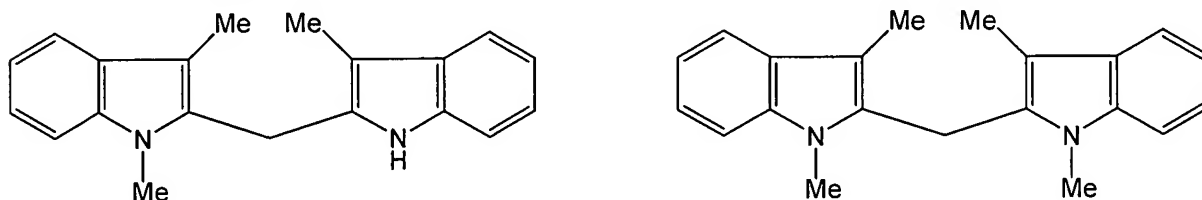
Claims 14-24 and 54-58 stand rejected under 35 U.S.C. §102 as being anticipated by Black et al., the Examiner citing the compound 1H-Indole-7-carboxaldehyde, 2,2'-methylenebis[4,6-dimethoxy-3-phenyl-, which has the structure:



The currently prosecuted claims do not read on the cited compound. As amended, one of the provisos of claim 14 (and thus all claims depending from claim 14) requires that at least one of R^2 and R^6 be other than hydrogen. For the compound in Black, both R^2 and R^6 represent hydrogen. Accordingly, Black does not anticipate any of the claims of the application, and removal of the rejection is respectfully requested.

Rejection under 35 U.S.C. § 102

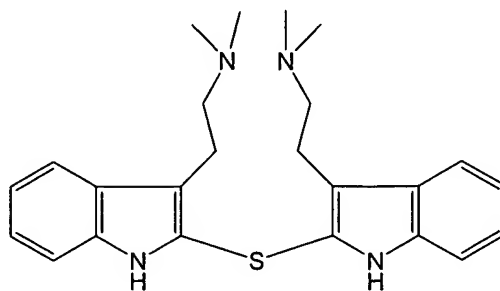
Claims 14-24 and 54-58 stand rejected under 35 U.S.C. §102 as being anticipated by Pindur et al., the Examiner citing the two compounds 1H-Indole, 2,2'-methylenebis[1,3-dimethyl-, and 1H-Indole, 1,3-dimethyl-2-[(3-methyl-1H-indol-2-yl)methyl]-, which have the following structures:



The present claims do not read on the compounds discussed in Pindur. The variables R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , and R^8 all represent hydrogen for each of the compounds from the reference, whereas one of the provisos of claims 14-24 and 54-58 of the application requires that at least one of R^2 and R^6 be other than hydrogen. Accordingly, Pindur does not anticipate any of the claims of the application, and applicants respectfully request removal of the rejection.

Rejection under 35 U.S.C. § 102

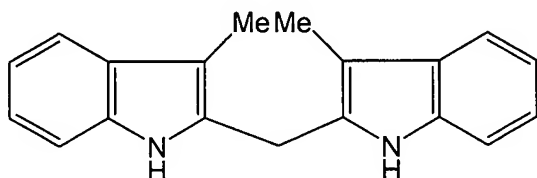
Claims 14-24 and 54-58 stand rejected under 35 U.S.C. §102 as being anticipated by Chu et al., the Examiner citing the compound 1H-Indole-3-enthaneamine, 2,2'-thiobis[N,N-dimethyl-, monohydrochloride, which has the structure:



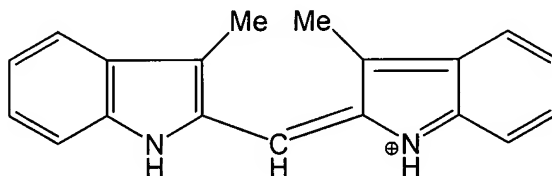
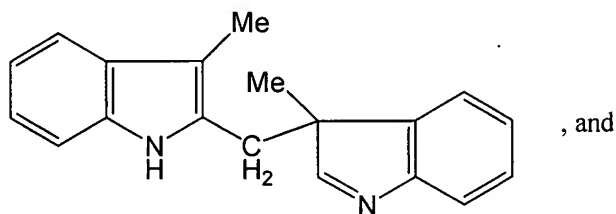
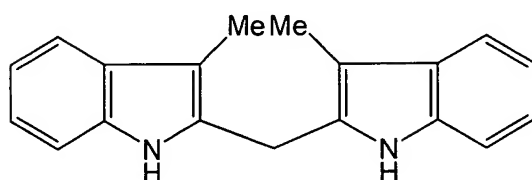
The present claims do not read on the compound discussed in Chu. The variables R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , and R^8 all represent hydrogen for the compound cited by the Examiner, whereas one of the provisos of claims 14-24 and 54-58 of the application requires that at least one of R^2 and R^6 be other than hydrogen. Accordingly, Chu does not anticipate any of the claims currently under prosecution, and removal of the rejection is respectfully requested.

Rejection under 35 U.S.C. § 102

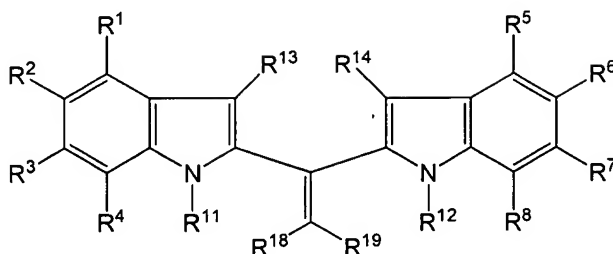
Claims 14-24 and 54-58 stand rejected under 35 U.S.C. §102 as being anticipated by Brieskorn et al., the Examiner citing the compound 1H-Indole, 2,2'-methylenebis[3-methyl-, which has the structure:



plus three additional compounds with the following structures:



The Examiner's rejection is not clear, as the first two compounds cited by the Examiner appear to be identical. Notwithstanding this uncertainty, the present claims do not read on the compounds specified in Brieskorn. The variables R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , and R^8 all represent hydrogen for each of the cited compounds, whereas one of the limitations of claims 14-24 and 54-58 of the application as presently amended requires that at least one of R^2 and R^6 be other than hydrogen. In addition, the third compound cited by the Examiner contains a [2,3]-connectivity for the indole moieties, which is different from the [2,2]-connectivity of the compounds of the currently prosecuted claims. Considering the fourth compound cited by the examiner, the bridging moiety between the indole moieties, represented by variable X in the application, is $(-CH=)$. The currently prosecuted claims, however, do not include $(-CH=)$ as a possibility for X. The "closest" structure for X is $CR^{15}R^{16}$, wherein R^{15} and R^{16} together form $=CR^{18}R^{19}$ where R^{18} and R^{19} are hydrogen or C_1 - C_6 alkyl, which has the structure

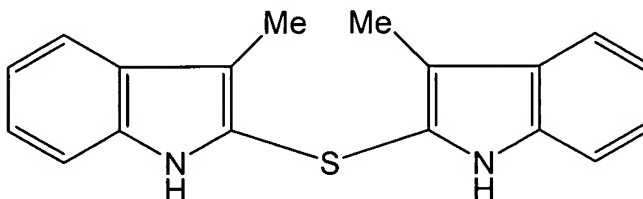


The carbon-carbon double bond geometry in the claims of the application is clearly distinct from the fourth compound cited by the Examiner.

Accordingly, the compounds from Brieskorn cited by the Examiner do not anticipate the claimed invention, and removal of the rejection is respectfully requested.

Rejection under 35 U.S.C. § 102

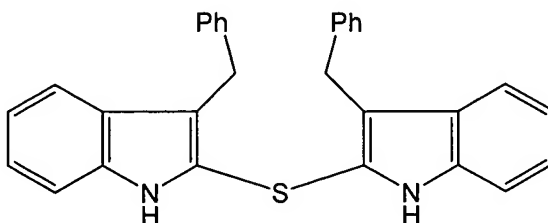
Claims 14-24 and 54-58 stand rejected under 35 U.S.C. §102 as being anticipated by Hindo et al., the Examiner citing a compound 1H-Indole, 2,2'-thiobis[3-methyl-.



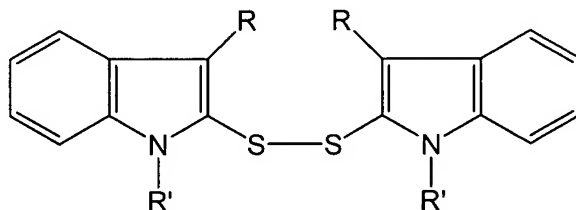
The present claims do not read on the compound cited in Hindo. The variables R¹, R², R³, R⁴, R⁵, R⁶, R⁷, and R⁸ all represent hydrogen for the compound discussed by Hindo, whereas one of the provisos of claims 14-24 and 54-58 of the application requires that at least one of R² and R⁶ be other than hydrogen. Accordingly, Hindo does not anticipate the claimed invention, and removal of the rejection is respectfully requested.

Rejection under 35 U.S.C. § 102

Claims 14-24 and 54-58 stand rejected under 35 U.S.C. §102 as being anticipated by Suzuki et al., the Examiner citing a compound 1H-Indole, 2,2'-thiobis[3-(phenylmethyl)-, which has the formula



A thorough search of the reference failed to uncover the cited compound. Page 2741 of the reference states that "...the reaction of 3-phenyl and 3-(*p*-methoxyphenyl)-indole with S₂Cl₂ in methylene chloride gave a complicated result in contrast to the reaction in ether, and monosulfides, unknown compounds, besides disulfide were obtained" (emphasis added). Isolation, identification, or characterization of the obtained monosulfides are not reported in Suzuki, and it is therefore impossible to determine from the reference the structures of any monosulfide compounds that may have been produced by the reactions of the reference. All other diindole compounds in Suzuki are disulfides, with the general structure



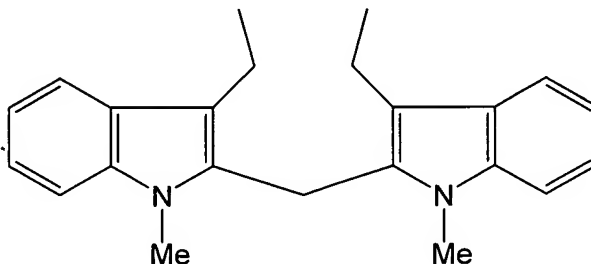
However, all of the compounds of the currently prosecuted claims are monosulfides, thus differing substantially from the disulfide compounds discussed by Suzuki.

Even if the monosulfides mentioned by Suzuki had been identified, the variables R¹, R², R³, R⁴, R⁵, R⁶, R⁷, and R⁸ represent hydrogen for all of the reagents and products in Suzuki. One of the provisos of claims 14-24 and 54-58 of the application requires that at least one of R² and R⁶ be other than hydrogen. Thus, the currently prosecuted claims do not read on any of the monosulfides that could have been produced in the reactions discussed by Suzuki.

Accordingly, Suzuki does not anticipate applicant's invention, and withdrawal of the rejection is respectfully requested.

Rejection under 35 U.S.C. § 102

Claims 14-24 and 54-58 stand rejected under 35 U.S.C. §102 as being anticipated by Hill et al., the Examiner citing a compound 1H-Indole, 2,2'-methylenebis[3-ethyl-1-methyl]-.



The present claims do not read on the compound cited by the Examiner. The variables R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , and R^8 all represent hydrogen for the compound discussed in Hill, whereas one of the provisos in the currently prosecuted claims 14-24 and 54-58 of the application requires that at least one of R^2 and R^6 be other than hydrogen. Accordingly, Hill does not anticipate applicant's invention, and removal of the rejection is respectfully requested.

Claim Objections

Claims 14-24 and 54-58 are objected to as containing non-elected subject matter, the Examiner citing the portions of the claims that refer to "5- or 6-membered cyclic rings or fused five-membered and/or six-membered ring, or heteroaromatic ring having heteroatoms, or heteroalicyclic ring having heteroatoms, heteroarylene of variable X, etc."

The objection is not well taken because the Patent and Trademark Office has no authority to require the applicant to narrow claims, rather than electing between claims, as part of a restriction requirement based on 35 USC 121. The prior restriction requirement (page 2) expressly stated that it was based on 35 USC 121. The CCPA held long ago that "§ 121 could not be used as the basis for rejecting a *single* claim or compelling its replacement by a plurality of narrower claims before examination on the merits would be made." *In re Harnisch*, 631 F.2d 716 (CCPA 1980). *Harnisch* remains binding authority and forbids an objection based on the restriction requirement of 12/10/04.

While *Harnisch* suggested that an "improper Markush group" rejection (**not** a 35 USC 121 restriction requirement) might be possible in some cases, the "improper Markush group" rejection contemplated by *Harnisch* is subject to very stringent requirements set out in that case, which are not met here. In particular, the inventions represented by the different elements of the Markush group at issue should be "*unrelated* inventions" which are "truly independent *and* distinct." 206 USPQ at 306. That is not the case here. There are structural relationships between the compounds encompassed by the generic claims since they are indole-3-carbinol metabolite analogs. The compounds are disclosed to have a common utility, the treatment of hyperproliferative diseases. The inventions which the elements of the Markush group relate to here are thus not unrelated or independent.


For the reasons given above, the Examiner is therefore requested to withdraw the objections to claims 14-24 and 54-58.

Conclusion

Applicants respectfully submit that the pending claims are in condition for allowance, and request such action.

Should the Examiner have any questions concerning the application, or the foregoing amendments and remarks, a telephone call to the undersigned at 650-251-7724 would be appreciated.

Respectfully submitted,

By: 
Isaac M. Rutenberg
Registration No. 57,419

REED IP LAW GROUP
1400 Page Mill Road
Palo Alto, California 94304
(650) 251-7710 Telephone
(650) 251-7739 Facsimile